IN THE MATTER of US
Patent Application No. 09/888,959
in the name of University of Sydney

This is **Exhibit RIC-1** referred to in the Statutory Declaration of Professor Richard Ian Christopherson made on 10 February 2004 (date).

R. I. Christopherson

Curriculum Vitae of Professor Richard I. Christopherson

School of Molecular and Microbial Biosciences
University of Sydney
Sydney
NSW 2006

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(a) Pers nal Details

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Born:	7th August, 1949, at Melbourne, Victoria
Citizenship:	Australian
Married:	Wife, Julie; children, Sascha (26 years) and James (21 years).
Memberships:	Corresponding Member of the American Association for Cancer Research (AACR, 1995-) Scientific Advisory Committee of the International Purine and Pyrimidine Society (2003-) National Committee for Biochemistry of the Australian Academy of Science (1991-97). Honorary Medical Officer, Royal North Shore Hospital (1995-) Australian Society for Biochemistry and Molecular Biology (ASBMB) Director, Medsaic Pty. Ltd. (2003-) Alternate Director and member of the Executive, Australian Proteome Analysis Facility (APAF) Director, Biomedical Node of APAF (University of Sydney)

(b) Degrees

1970	Bachelor of Science from the University of Melbourne majoring in Biochemistry and Chemistry.
1973-76 (May)	Doctor of Philosophy (Biochemistry) from the University of Melbourne; thesis entitled "Interrelationships of Pyrimidine Biosynthesis in *Escherichia coli* K12".

(c) Appointments

1971-72	Tutor (full-time), Russell Grimwade School of Biochemistry, University of Melbourne.
1976-78 (July)	Fellow of the Damon Runyon-Walter Winchell Cancer Fund, Biochemistry Department, School of Medicine, University of Southern California, Los Angeles, USA.
1978-80 (June)	Special Fellow of the Leukemia Society of America, Biochemistry Department, School of Medicine, University of North Carolina at Chapel Hill, USA.
1980-83 (January)	Research Fellow, Biochemistry Department, John Curtin School of Medical Research, Australian National University.
1983-86 (January)	C.R. Roper Fellow in Medical Research, Russell Grimwade School of Biochemistry, University of Melbourne.
1986-97	Lecturer/Senior Lecturer/Associate Professor, Department of Biochemistry, University of Sydney.

1998-03	Professor (Personal Chair) and Head, Department of Biochemistry/School of Molecular and Microbial Biosciences, University of Sydney.
2004-	Professor (Personal Chair), School of Molecular and Microbial Biosciences, University of Sydney.

(d) Research

(i) Grants Received (Total 1987-03: $7,202,162)

1987	
NH&MRC	33,461
ARGS	5,000
Utah Foundation	24,000
University of Sydney Cancer Research Fund	10,000
Wellcome Australia Ltd.	121,482
	$193,943
1988	
NH&MRC	34,693
NH&MRC	24,833
ARC	6,000
Wellcome Australia Ltd.	122,960
	$188,486
1989	
NH&MRC	35,810
NH&MRC	25,876
ARC	8,000
Wellcome Australia Ltd.	133,928
	$203,614
1990	
NH&MRC	37,827
ARC	8,394
Wellcome Australia Ltd.	159,129
University of Sydney Cancer Research Fund	18,000
Leo & Jenny Leukaemia & Cancer Foundation	10,000
NSW State Cancer Council (with Prof. B.D. Roufogalis)	40,174
	$273,524
1991	
NH&MRC	39,869
University of Sydney Cancer Research Fund	8,000
USCRF (with Prof. B.D. Roufogalis)	46,795
Leo & Jenny Leukaemia & Cancer Foundation	40,099
University of Sydney major equipment grant	30,000
Department of Biochemistry equipment grant	9,000
	$173,763
1992	
World Health Organization	68,435
NH&MRC	92,092
University of Sydney Cancer Research Fund	42,252
Parnell Laboratories (clinical trial analyses)	26,100
	$228,879
1993	
NH&MRC	95,849
NH&MRC	41,660
Leo & Jenny Leukaemia & Cancer Foundation	40,000
World Health Organisation (US$52,137)	75,742
University of Sydney Cancer Research Fund	42,252
	$295,503
1994	
NH&MRC	96,904
NH&MRC	42,118
World Health Organisation (US$65,137)	98,692
University of Sydney Cancer Research Fund	42,252
ARC small grant	8,000
	$287,966

	Prof RJ Christopherson
1995	
NH&MRC	42,792
NH&MRC	58,258
WHO	46,052
ARC	8,000
	$155,102
1996	
NH&MRC	58,258
University of Sydney infrastructure funds	53,933
University of Sydney Cancer Research Fund	45,000
ARC small grant	8,000
	$165,191
1997	
NH&MRC	61.951
NH&MRC equipment grant (with C. Collyer & G. King)	25,000
ARC RIEFP grant (with C. Collyer)	185,000
University of Sydney Cancer Research Fund	45,000
Faculty of Medicine	15,000
	$331,951
1998	
Wellcome Trust (Recombinant Protein Facility)	172,388
Faculty of Medicine	10,000
Ramaciotti Foundation (with P.W. Kuchel)	25,000
	$207,388
1999	
Wellcome Trust	172,388
ARC Institutional Grant	9,500
Enterix Pty. Ltd.	125,936
	$307,824
2000	
Enterix (with C.G. dos Remedios)	300,469
Wellcome Trust	172,388
ARC Small Grant	23,000
U2000 Fellowship (to M.A. Kamal)	63,953
	$559,810
2001	
Wellcome Trust	172,388
U2000 Fellowship (to M.A. Kamal)	63,953
U2000 Fellowship (to R.I. Menz)	31,976
COMET grant (with C.G. dos Remedios, J. Chrisp)	25,000
	$293,317
2002	
USyd Sesqui grant	40,000
AusIndustry Business Innovation Fund (with C dos Remedios, J Chrisp and B Hamdorf)	500,000
AusIndustry COMET grant (with C dos Remedios, J Chrisp and B Hamdorf)	25,000
Wellcome Trust Major Equipment Grant	14,000
USyd U2000 Fellowship (to MA Kamal)	63,953
	$642,953
2003	
USyd Sesqui, Equipment (with RC Baxter, R Christopherson and N King)	208,000
AusIndustry, Major National Research Facility, Australian Proteome Analysis Facility (with P Bergquist *et al.*)	1,790,000
NH&MRC	80,000
Medsaic (spin-off company, CEO J Chrisp)	239,421
Medsaic	83,821
Medsaic	259,730
USyd U2000 Fellowship (to MA Kamal)	31,976
	$2,692,948

2004 (incomplete)	
USyd Sesqui, Equipment (with M. Crossley, K. Downard, R. Overall, W. Britton, J Triccas, N Jacques, A. Weiss)	70,000
NH&MRC	70,000
ARC (with R Baxter)	90,000
ARC LIEF for MALDI-TOF/TOF mass spectrometer (with J. Gorman UQ)	1,649,750
Medsaic (spin-off company, CEO J Chrisp)	to be determined

(ii) Research Group Members

Larissa Belov PhD	Research Fellow
Peter Ellmark PhD	Postdoctoral Fellow
Pauline Huang MSc	Research Assistant
Camilla Chan BSc(Hons)	Research Assistant
Nicole Barber BSc(Hons)	PhD student
Carlos Cassano BSc(Hons)	PhD student
Maryam Shojaei BSc(Hons)	PhD student
Louise Bransgrove BSc(Hons)	PhD student
Silke Henrich	PhD student
Daniel Morgan	BSc(Hons) student
Stephen P Mulligan PhD MBBS FRACP	Adjunct Senior Lecturer
Jeremy Chrisp PhD	CEO, Medsaic Pty. Ltd.

(iii) Research Projects

1. *Leukaemia membrane proteomics.* Procedures have been developed for sub-cellular fractionation of leukocytes. Plasma membrane and nuclear proteomes will be determined for leukaemia cell lines treated with various drugs, and leukaemia cells from patients.

2. *Immunophenotyping solid tumours.* Biopsies of colon cancer have been reduced to single cell suspensions and a procedure has been developed for getting the cells to re-express intact surface molecules. An antibody microarray is under development for immunophenotyping cells from colon cancer , initially using human cell lines.

3. *Direct immunophenotyping of whole blood lysates.* The current procedure used for immunophenotyping leukocytes from blood samples is to purify them by Histopaque centrifugation which also removes a major proportion of the predominant neutrophils. The leukocytes are then specifically captured on a CD antibody microarray. Leukocytes can be analyzed directly by flow cytometry following selective lysis of erythrocytes. We propose to develop a protocol which enables blood lysates to be analyzed using the CD antibody microarray in the presence of the predominant neutrophils.

4. *Detection of intracellular antigens in captured cells.* Leukocytes captured on a CD antibody microarray will be permeabilised and probed with soluble, fluorescently-labelled antibodies against intracellular protein markers such as p210, which is associated with chronic myeloid leukaemia (CML) and acute lymphocytic leukaemia (ALL). p210 is a tyrosine kinase that is inhibited by the novel anticancer drug, Glivec.

5. *A database for leukaemias and lymphomas.* Statistical analysis of sub-types (e.g. AML) using principal component plots will be prepared from the more than 300 immunophenotypes already determined for a variety of leukaemias and lymphomas from patients. Such plots show segregation of disease types in component space and should show that an extensive immunophenotype provides sufficient information for diagnoses.

6. Development of recombinant antibodies. The CD antibody microarray will detect unusual pairs of antigens expressed on particular leukaemias. Antibody-like molecules have been designed that will only kill cells expressing an unusual pair of CD antigens.

7. *Cloning and expression of malarial pyrimidine pathway enzymes.* In collaboration with Dr Ian Menz, now at Flinders University, we have cloned the malarial genes encoding dihydroorotase, orotate phosphoribosyltransferase, and OMP decarboxylase. We have obtained cloned genes for carbamyl phosphate synthetase, aspartate transcarbamylase and CTP synthetase from collaborators at the University of NSW. We are over-expressing and purifying these enzymes, and growing protein crystals for determination of their three-dimensional structures.

8. *The catalytic mechanisms of dihydroorotases.* Enzymes from hamster, *P. falciparum*, *Bacillus caldolyticus* and *Escherichia coli.* These enzymes have been cloned, over-expressed and purified, and comparative kinetic analyses are underway. We are also characterizing Type 1 and 2 dihydroorotases which may have one and two zinc atoms, respectively, at their active sites.

(iv) Key Research Discoveries

1. *Expression of hamster dihydroorotase.* The central DHOase domain of the trifunctional protein, DHO synthetase, has been cloned, sequenced, expressed in *E. coli*, purified in hundreds of milligrams and crystallised. We have published a low resolution X-ray structure.

2. *The catalytic mechanism of dihydroorotase.* We have shown there is a zinc atom at the active site coordinated by 3 histidine residues which participates in catalysis. Site-directed mutagenesis and kinetic experiments have enabled elucidation of the catalytic mechanism of DHOase.

3. *Inhibitors of dihydroorotase.* A series of potent inhibitors of DHOase has been rationally designed from a knowledge of the catalytic mechanism of the enzyme. TDHO (K_i = 0.85 μM) may be regarded as a chelating inhibitor, while HDDP (K_i = 0.74 μM) and OAPC (K_i = 7.4 μM) are transition-state analogues. Alkyl esters of TDHO and HDDP induce inhibition of DHOase and hence *de novo* pyrimidine biosynthesis in leukaemia cells and malaria growing in culture with IC_{50} values of less than 20 μM.

4. *The mechanism of the anti-purine effect of methotrexate.* We have found that the high levels of dihydrofolate polyglutamates induced by methotrexate in leukaemia cells inhibit amido phosphoribosyltransferase catalysing the first step of the *de novo* purine pathway. Dihydrofolate polyglutamates and some other folate derivatives such as piritrexim bind at a new inhibitory allosteric site on this enzyme and induce formation of an inactive 7.2 S dimer rather than the inactive 10.2 S tetramer induced by purine nucleoside monophosphates. Elucidation of the true antipurine effect of methotrexate is very important because this antifolate is used to treat leukaemia, breast cancer, rheumatoid arthritis and lupus.

Preliminary data suggest that the antifolate, Lometrexol, which is known to inhibit the third reaction of the *de novo* purine pathway, also inhibits amido phosphoribosyltransferase (reaction 1) which would be the primary blockade of purine biosynthesis.

5. *Measurement of 2'-deoxynucleoside-5'-triphosphates in malaria and fresh human leukaemia cells.* We have developed HPLC procedures which enable the direct measurement of dNTPs in cells taken from patients with Chronic Lymphocytic Leukaemia (CLL) enabling a detailed investigation of the mechanisms of action of the drugs cladribine, fludarabine and pentostatin. These techniques have also been used to measure dNTPs in the malarial parasite, *Plasmodium falciparum,* growing in erythrocytic culture. We have found that the antifolate, WR99210, inhibits dihydrofolate reductase in the parasite but there is an additional site of action which remains to be determined. Parasites exposed to a variety of drugs and orotate maintain relatively constant levels of dCTP suggesting that this dNTP is compartmentalised or that its levels are maintained via unknown regulatory mechanisms.

6. *AICAR transformylase-IMP cyclohydrolase.* The bifunctional enzyme AICAR transformylase-IMP cyclohydrolase has been purified to homogeneity from human leukaemia cells. A purine nucleoside monophosphate analogue (MIMP) has been synthesised which is a potent inhibitor of IMP cyclohydrolase ($K_i = 94$ nM).

7. *A CD antibody microarray.* This microarray of immobilized antibodies against surface molecules found on cells provides extensive immunophenotypes of leukocytes and cells from solid tissues. Using this novel technique, consensus immunophenotypes have been established for the common leukaemias. We have proposed that an extensive immunophenotype should be sufficient to diagnose leukaemias without using additional criteria of cell morphology, cytochemistry and cytogenetics. A scanner and software have been developed by a spin-off company, Medsaic, and a diagnostic kit for leukaemias will be marketed in late 2003.

(v) Collaborators

1. Immunophenotyping leukaemias from patients using a CD antibody microarray. Dr. S.P. Mulligan, Department of Haematology, Concord Hospital.

2. Proteomic analysis of breast cancer cells undergoing apoptosis. Prof R Baxter, Kolling Institute of Medical Research, Royal North Shore Hospital, Sydney.

3. Analysis of subpopulations of normal germinal center B cells, memory and naive B cells using a CD antibody microarray. Prof. Carl A.K. Borrebaeck, Department of Immunotechnology, Lund University, Sweden.

4. Cloning, expression, purification, crystallization and structural determination of enzymes from the *de novo* pyrimidine pathway in the malarial parasite, *P. falciparum.* Dr R Ian Menz, School of Biological Sciences, Flinders University.

5. Protein crystallography with recombinant hamster and bacterial dihydroorotases and malarial OMP decarboxylase. Drs M. Maher, D. Langley and M. Guss, School of Molecular and Microbial Biosciences, University of Sydney.

6. Membrane proteomics of leukaemia cell lines and leukaemias from patients. Prof Mark Baker and Dr Stuart Cordwell, Australian Proteome Analysis Facility, Macquarie University.

(e) Publications

(i) Articles in Refereed Journals

1. Christopherson, R.I. & Finch, L.R. (1976) Anal. Biochem. 73, 342-349. A radioisotopic method for the assay of aspartate carbamoyltransferase and carbamoyl phosphate.
2. Christopherson, R.I. & Finch, L.R. (1977) Biochem. Biophys. Acta 481, 80-85. Regulation of aspartate carbamoyltransferase of *Escherichia coli* by the interrelationship of magnesium and nucleotides.
3. Christopherson, R.I. & Finch, L.R. (1977). Anal. Biochem. 80, 159-167. The assay of orotate by an isotope dilution procedure.
4. Christopherson, R.I. & Finch, L.R. (1978). Eur. J. Biochem. 90, 347-358. Responses of the pyrimidine pathway of *Escherichia coli* K12 to exogenous adenine and uracil.
5. Christopherson, R.I., Matsuura, T. & Jones, M.E. (1978) Anal. Biochem. 89, 225-234. Radioassay of dihydroorotase utilizing ion-exchange chromatography.
6. Christopherson, R.I., Jones, M.E. & Finch, L.R. (1979) Anal. Biochem. 100, 184-187. A simple centrifuge column for desalting protein solutions.
7. Christopherson, R.I. & Jones, M.E. (1979) J. Biol. Chem. 254, 12506-12512. Interconversion of carbamyl-L-aspartate and L-dihydroorotate by dihydroorotase from mouse Ehrlich ascites carcinoma.
8. Christopherson, R.I. & Jones, M.E. (1980) J. Biol. Chem. 255, 3358-3370. The effects of pH and inhibitors upon the catalytic activity of the dihydroorotase of multienzymatic protein *pyrl-3* from mouse Ehrlich ascites carcinoma.
9. Christopherson, R.I. & Jones, M.E. (1980) J. Biol. Chem. 255, 11381-11395. The overall synthesis of L-5,6-dihydroorotate by multienzymatic protein *pyrl-3* from hamster cells. Kinetic studies, substrate channeling, and the effects of inhibitors.
10. Christopherson, R.I., Yu, M.-L. & Jones, M.E. (1981) Anal. Biochem. 111, 240-249. An overall radioassay for the first three reactions of *de novo* pyrimidine biosynthesis.
11. Christopherson, R.I. & Morrison, J.F. (1983) Arch. Biochem. Biophys. 220, 444-450. Synthesis and separation of tritium-labelled intermediates of the shikimate pathway.
12. Christopherson, R.I., Heyde, E. & Morrison, J.F. (1983) Biochemistry 22, 1650-1656. Chorismate mutase-prephenate dehydrogenase from *Escherichia coli*: Spatial relationship of the mutase and dehydrogenase sites.
13. Christopherson, R.I. & Duggleby, R.G. (1983) Eur. J. Biochem. 134, 331-335. Metabolic resistance: The protection of enzymes against drugs which are tight-binding inhibitors by the accumulation of substrate.
14. Duggleby, R.G. & Christopherson, R.I. (1984) Eur. J. Biochem. 143, 221-226. Metabolic resistance to tight-binding inhibitors of enzymes involved in the *de novo* pyrimidine pathway: Simulation of time-dependent effects.
15. Lyons, S.D. & Christopherson, R.I. (1985) Eur. J. Biochem. 147, 587-592. Regulation of hamster carbamyl phosphate synthetase II by 5-phosphoribosyl-1-pyrophosphate and uridine 5'-triphosphate.
16. Christopherson, R.I. & Morrison, J.F. (1985) Biochemistry 24, 1116-1121. Chorismate mutase-prephenate dehydrogenase from *Escherichia coli*: Positive cooperativity with substrates and inhibitors.
17. Christopherson, R.I. (1985) Arch. Biochem. Biophys. 240, 646-654. Chorismate mutase-prephenate dehydrogenase from *Escherichia coli*: Cooperative effects and inhibition by L-tyrosine.
18. Kemp, A.J., Lyons, S.D. & Christopherson, R.I. (1986) J. Biol. Chem., 261, 14891-14895. Effects of acivicin and dichloroallyl lawsone upon pyrimidine biosynthesis in mouse L1210 leukemia cells.
19. Herd, S.M., Camakaris, J., Christopherson, R.I., Wookey, P. & Danks, D.M. (1987) Biochem. J. 247, 341-347. Uptake and efflux of copper-64 in Menkes' disease and normal continuous lymphoid cell lines.
20. Christopherson, R.I., Schmalzl, K.J., Szabados, E., Goodridge, R.G., Harsanyi, M.C., Sant, M.E., Algar, E.M., Anderson, J.E., Armstrong, A., Sharma, S.C., Bubb, W.A. & Lyons, S.D. (1989) Biochemistry, 28, 463-470. Mercaptan and dicarboxylate inhibitors of hamster dihydroorotase.
21. Sant, M.E., Lyons, S.D., Kemp, A.J., McClure, L.K., Szabados, E. & Christopherson, R.I. (1989) Cancer Res. 49, 2645-2650. Dual effects of pyrazofurin and 3-deazauridine upon pyrimidine and purine biosynthesis in mouse L1210 leukemia.
22. Gero, A.M., Scott, H.V., O'Sullivan, W.J. & Christopherson, R.I. (1989) Mol. Biochem. Parasitol. 34, 87-98. The antimalarial action of nitrobenzyl thioinosine in combination with purine nucleoside anti-metabolites.
23. Sant, M.E., Poiner, A., Harsanyi, M.C., Lyons, S.D. & Christopherson, R.I. (1989) Anal. Biochem. 182, 121-128. Chromatographic analysis of purine precursors in mouse L1210 leukemia.
24. Becker, K., Christopherson, R.I., Cowden, W.B., Hunt, N.H. & Schirmer, R.H. (1989) Biochem. Pharmacol. 39, 59-65. Flavin analogues with antimalarial activity as glutathione reductase inhibitors.

25. Lewis, P.J., Ralston, G.B., Christopherson, R.I. & Wake, R.G. (1990) J. Mol. Bi l., 214, 73-84. Identification of the replication terminator protein binding sites in the terminus region of the *Bacillus subtilis* chromosome and stoichiometry of the binding.
26. Lyons, S.D., Sant, M.E. & Christopherson, R.I. (1990) J. Biol. Chem., 265, 11377-11381. Cytotoxic mechanisms of glutamine antagonists in mouse L1210 leukemia.
27. Williams, N., Simpson, R.J., Moritz, R.L., Peide, Y., Crofts, L., Minasian, E., Leach, S.J., Wake, R.G. & Christopherson, R.I. (1990) Gene, 94, 283-288. Location of the dihydroorotase domain within trifunctional hamster dihydroorotate synthetase.
28. Crofts, L., Peide, Y., Woodhouse, A., Algar, E.M. & Christopherson, R.I. (1990) Prot. Exp. Purif., 1, 45-48. Purification of hamster dihydroorotate synthetase using Procion Blue-Sepharose.
29. Shostak, K., Christopherson, R.I. & Jones, M.E. (1990) Anal. Biochem., 191, 365-369. Direct spectrophotometric assays for orotate phosphoribosyltransferase and orotidylate decarboxylase.
30. Brooke, J.H., Szabados, E., Lyons, S.D. & Christopherson, R.I. (1990) Cancer Res., 50, 7793-7798. Cytotoxic effects of dihydroorotase inhibitors upon human CCRF-CEM leukaemia.
31. Lyons, S.D. & Christopherson, R.I. (1990) Biochem. Int., 22, 939-949. Effects of brequinar and ciprofloxacin on *de novo* nucleotide biosynthesis in mouse L1210 leukemia.
32. Berners-Price, S.J., Sant, M.E., Christopherson, R.I. & Kuchel, P.W. (1991) Mag. Res. Med., 18, 142-158. ^{1}H and ^{31}P NMR and HPLC studies of mouse L1210 leukaemia cells. The effect of Au(I) and Cu(I) diphosphine complexes on the cell metabolism.
33. Szabados, E. & Christopherson, R.I. (1991) Biochemical Education, 19, 90-94. Adenosine deaminase deficiency in erythrocytes.
34. Christopherson, R.I. & Williams, N.K. (1991) Today's Life Science 3, 20-27. The design of anticancer drugs.
35. Lyons, S.D. & Christopherson, R.I. (1991) Biochem. Int. 24, 187-197. Antifolates inhibit the *de novo* purine pathway prior to 5-aminoimidazole-4-carboxamide ribotide transformylase in leukemia cells.
36. Schöbitz, B., Wolf. S., Christopherson, R.I. & Brand, K. (1991) Biochim. Biophys. Acta, 1095, 95-102. Nucleotide and nucleic acid metabolism in rat thymocytes during cell cycle progression.
37. Sant, M.E., Lyons, S.D., Phillips, L. & Christopherson, R.I. (1992) Pteridines 3, 133-134. Inhibition of amido phosphoribosyltransferase by antifolates in mouse L1210 leukaemia cells.
38. Sant, M.E., Lyons, S.D., Phillips, L. & Christopherson, R.I. (1992) J. Biol. Chem. 267, 11038-11045. Antifolates induce inhibition of amido phosphoribosyltransferase in leukemia cells.
39. Christopherson, R.I. & Seymour, K.K. (1992) Today's Life Science 4, 66-74. Capillary electrophoresis.
40. Hambley, T.W., Phillips, L., Poiner, A.C. & Christopherson, R.I. (1993) Acta Cryst. B49, 130-136. A crystallographic and molecular mechanics study of inhibitors of dihydroorotase.
41. Williams, N., Piede, Y., Seymour, K.K., Ralston, G.B. & Christopherson, R.I. (1993) Prot. Eng. 6, 333-340. Expression of catalytically-active hamster dihydroorotase domain in *Escherichia coli*: Purification and characterization.
42. Syed, S.K., Christopherson, R.I. & Roufogalis, B.D. (1993) Biochem. Mol. Biol. Intl. 30, 743-753. Vinblastine transport by membrane vesicles from human multidrug-resistant CCRF-CEM leukaemia cells: Inhibition by taxol and membrane permeabilising agents.
43. Seymour, K.K., Lyons, S.D., Phillips, L. & Christopherson, R.I. (1994) Biochemistry 33, 5268-5274. Cytotoxic effects of inhibitors of *de novo* pyrimidine biosynthesis upon *Plasmodium falciparum*.
44. Cao, Y., Christopherson, R.I., Elix, J.A. & Gaul, K.L. (1994) Aust. J. Chem. 47, 903-911. Synthesis of a phosphinic acid transition state analogue inhibitor of dihydroorotase.
45. Jeitner, T.W., Kneale, C.L., Christopherson, R.I. & Hunt, N.H. (1994) Biochim. Biophys. Acta. 1223, 15-22. Thiol-bearing compounds selectively inhibit protein kinase C-dependent oxidative events and proliferation in human T cells.
46. Szabados, E., & Christopherson, R.I. (1994) Anal. Biochem., 221, 401-404. Assay of bifunctional AICAR transformylase-IMP cyclohydrolase by thin-layer chromatography.
47. Szabados, E., Hindmarsh, E., Phillips, L., Duggleby, R.G. & Christopherson, R.I. (1994) Biochemistry 33, 14,237-14,245. 5-Aminoimidazole-4-carboxamide ribotide transformylase-IMP cyclohydrolase from human CCRF-CEM leukemia cells: Purification, pH dependence and inhibitors.
48. Schoettle, S.L. & Christopherson, R.I. (1995) Purine and Pyrimidine Metabolism in Man VIII (Sahota, A. & Taylor, M.W., eds.), pp 151-154, Plenum Press, New York. Inhibition of murine amido phosphoribosyltransferase by folate derivatives.
49. Williams, N.K., Isaac, E.L., Yin, P. & Christopherson, R.I. (1995) Purine and Pyrimidine Metabolism in Man VIII (Sahota, A. & Taylor, M.W., eds.), pp 549-553, Plenum Press, New York. The catalytic mechanism of hamster dihydroorotase.
50. Williams, N.K., O'Donoghue, S. & Christopherson, R.I. (1995) Purine and Pyrimidine Metabolism in Man VIII (Sahota, A. & Taylor, M.W., eds.), pp 597-601, Plenum Press, New York. Homology and mutagenesis studies of hamster dihydroorotase.
51. Szabados, E. & Christopherson, R.I. (1995) J. Chromatog. B: Biomed. Appl., 674, 132-137. A rapid radioassay for metabolites of adenosine and deoxyadenosine in erythrocytes.

52. Hambley, T.W., Christopherson, R.I. & Zvargulis, E.S. (1995) J. Inorg. Chem., 34, 6550-6552. Models of the active site of dihydroorotase: The structure of bisaquabis (L-dihyroorotato) zinc(II) reveals an unexpected coordination mode for the L-dihydroorotato ligands.
53. Williams, N.K., Manthey, M.K., Hambley, T.W., O'Donoghue, S.I., Keegan, M., Chapman, B.E. & Christopherson, R.I. (1995) Biochemistry, 34, 11344 -11352. Catalysis by hamster dihydroorotase: zinc binding, site-directed mutagenesis and interaction with inhibitors.
54. Musk, P., Clark, J., Dunn, I.S., Christopherson, R.I., Szabados, E., Rose, S. & Parsons, P.G. (1996) Mutation Res. 350, 229-238. Purine deoxynucleoside metabolism in human melanoma cells with a high spontaneous mutation rate.
55. Syed, S.K., Christopherson, R.I. & Roufogalis, B.D. (1996) Biochem. Mol. Biol. Intl. 39, 687-696. Chlorpromazine transport in membrane vesicles from multidrug resistant CCRF-CEM leukaemia cells.
56. Christopherson, R.I. (1996) Aust. J. Nut. Diet. 53, S8-S10. How folate functions inside the body.
57. Crisp, L.B., Smith, S.M., Mathers, M.A.G., Young, G.A.R., Lyons, S.D. & Christopherson, R.I. (1996) Int. J. Biochem. Cell. Biol., 28, 1061-1069. Effects of cytosine arabinoside on human leukemia cells.
58. Szabados, E., Duggleby, R.G. & Christopherson, R.I. (1996) Int. J. Biochem. Cell. Biol. 28, 1405-1414. Metabolism of adenosine and deoxyadenosine by human erythrocytes and CCRF-CEM leukemia cells.
59. Yeo, A.E.T., Seymour, K.K., Rieckmann, K.H. & Christopherson, R.I. (1997) Biochem. Pharmacol. 53, 943-950. Effects of dual combinations of antifolates with atovaquone or dapsone on nucleotide levels in *Plasmodium falciparum*.
60. Christopherson, R.I. (1997) Int. J. Biochem. Cell. Biol. 29, 589-594. Partial inactivation of chorismate mutase-prephenate dehydrogenase from *Escherichia coli* in the presence of analogues of chorismate.
61. Yeo, A.E.T., Seymour, K.K., Rieckmann, K.H. & Christopherson, R.I. (1997) Ann. Trop. Med. Parasitol. 91, 17-23. Effects of folic and folinic acids on the activities of cycloguanil and WR99210 against *Plasmodium falciparum* in erythrocytic culture.
62. Schoettle, S.L., Szabados, M. & Christopherson, R.I. (1997) Biochemistry 36, 6377-6383. Mechanisms of inhibition of amido phosphoribosyltransferase from mouse L1210 leukemia.
63. Carter, L.K., Christopherson, R.I. & dos Remedios, C.G. (1997) Electrophoresis 18, 1054-1058. Analysis of the binding of deoxyribonuclease I to G-actin by capillary electrophoresis.
64. Batty, C.A., Manthey, M.K., Kirk, J., Manthey, M. & Christopherson, R.I. (1997) J. Heterocyc. Chem. 34, 1355-1367. Synthesis and exchange reactions of 5-alkyl-2-oxo-6-thioxo-1,2,3,6-hexahydropyrimidine-4-carboxylic acids.
65. Seymour, K.K., Yeo, A.E.T., Rieckmann, K.H. & Christopherson, R.I. (1997) Ann. Trop. Med. Parasitol. 91, 603-609. dCTP levels are maintained in *Plasmodium falciparum* in pyrimidine deficiency or excess.
66. Christopherson, R.I., Seymour, K.K. & Yeo, A.E.T. (1998) Purine and Pyrimidine Metabolism in Man IX (Griesmacher, A., Chiba, P. & Muller, M.M., eds.), Plenum Press, New York. Adv. Exp. Med. Biol. 431, 705-709. Pyrimidine antagonists and antifolates as antimalarial drugs.
67. Szabados, E. & Christopherson, R.I. (1998) Purine and Pyrimidine Metabolism in Man IX (Griesmacher, A., Chiba, P. & Muller, M.M., eds.), Plenum Press, New York. Adv. Exp. Med. Biol. 431, 241-244. Substrate channelling by human IMP synthase.
68. Yeo, A.E.T. & Christopherson, R.I. (1998) Ann. Trop. Med. Parasitol. 92, 331-333. Comparative effects of cycloguanil and WR99210 in malaria-infected erythrocytes and human leukaemia cells.
69. Yeo, A.E.T., Rieckmann, K.H. and Christopherson, R.I. (1998) S.E. Asian J. Trop. Med. Pub. Health 29, 24-26. Indirect inhibition by antibiotics of nucleotide and deoxynucleotide biosynthesis in *Plasmodium falciparum*.
70. Szabados, E., Manthey, M.K., Wilson, P.K. & Christopherson, R.I. (1998) Biochem. Mol. Biol. Int. 44, 617-23. Inosine-5'-monophosphate analogues as inhibitors of human IMP cyclohydrolase and cellular growth.
71. Szabados, E. & Christopherson, R.I. (1998) Int. J. Biochem. Cell. Biol. 30, 933-942. Relationship between the catalytic sites of human bifunctional IMP synthase.
72. Shi, R.Z., Lyons, S.D. & Christopherson, R.I. (1998) Int. J. Biochem. Cell Biol. 30, 885-895. Anticancer mechanisms of thiopurine derivatives against human CCRF-CEM leukaemia cells.
73. Wilson, P.K., Szabados, E., Mulligan, S.P. & Christopherson, R.I. (1998) Int. J. Biochem. Cell Biol. 30, 833-42. Comparative effects of cladribine, fludarabine and pentostatin on nucleotide metabolism in T- and B-cell lines.
74. Syed, S., Christopherson, R.I. & Roufogalis, B.D. (1998) Brit. J. Cancer, 78, 321-327. Reversal of vinblastine transport by chlorpromazine derivatives in membrane vesicles from multidrug resistant human CCRF-CEM leukaemia cells.
75. Manthey, M.K., Huang, D.T.C., Bubb, W.A. and Christopherson, R.I. (1998) J. Med. Chem. 41, 4550-4555. Synthesis and enzymic evaluation of 4-mercapto-6-oxo-1,4-azaphosphinane-2-carboxylic acid 4-oxide as an inhibitor of mammalian dihydroorotase.
76. Huang D.T., Thomas M.A., Christopherson R.I. (1999) Biochemistry 38, 9964-9970. Divalent metal derivatives of the hamster dihydroorotase domain.

77. Conigrave AD, van der Weyden L, Holt L, Jiang L, Wilson P, Christopherson RI, Morris MB. (2000) Biochem Pharmacol. 60, 1585-1591. Extracellular ATP-dependent suppression of proliferation and induction of differentiation of human HL-60 leukemia cells by distinct mechanisms.
78. Bel v L, de la Vega, dos Remedios CG, Mulligan SP and Christopherson RI (2001) Cancer Res. 61, 4483-4489. Immunophenotyping of Leukemias Using a Cluster of Differentiation Antibody Microarray.
79. Cinquin O, Christopherson RI, Menz RI. (2001) Mol Biochem Parasitol. 117, 245-247. A hybrid plasmid for expression of toxic malarial proteins in *Escherichia coli.*
80. Menz RI, Cinquin O, Christopherson RI (2002) Ann. Trop. Med. Parasitol. 96, 469-476. The identification, cloning and functional expression of the gene encoding orotidine 5'-monophosphate (OMP) decarboxylase from *Plasmodium falciparum.*
81. Maher MJ, Huang DTC, Guss JM, Collyer CA, Christopherson RI (2003) Acta Cryst. D59, 381-384. Crystallization of hamster dihydroorotase: involvement of a disulfide-linked tetrameric form.
82. Belov L, Huang P, Barber N, Mulligan SP, Christopherson RI (2003) Proteomics 3, 2147-2154. Identification of repertoires of surface antigens on leukaemias using an antibody microarray.
83. Christopherson RI, Cinquin O, Shojaei M, Kuehn D, Menz RI (2004) Nucleosides, nucleotides and nucleic acids, in press. Cloning and expression of malarial pyrimidine enzymes.
84. Kamal MA, Christopherson RI (2004) Int. J. Biochem. Cell Biol. 36, 545-551. Accumulation of 5-phosphoribosyl-1-pyrophosphate in human CCRF-CEM leukaemia cells treated with antifolates.
85. Wilson PK, Mulligan SP, Christopherson RI (2004) Leukemia Research, in press. Metabolic response patterns of nucleotides in B-cell chronic lymphocytic leukaemias to cladribine, fludarabine and deoxycoformycin.

(ii) Manuscripts Submitted

All accepted

(iii) Manuscript in Preparation

86. Huang DTC, Kaplan J, Menz RI, Karis VL, Wake RG, Anderson M, Cleland WW, Christopherson RI (2004) Biochemistry Catalysis by mesophilic and thermophilic dihydroorotases: Effects of temperature, inhibition and denaturation.
87. Lee, M, Guss, JM, Chan, C, Maher, M, and Christopherson, RI (2004) *E. coli* dihydroorotase: structure of the enzyme crystallised in the presence of dihydroorotate and cooperativity between subunits.

(iv) Chapters in Books

88. Christopherson, R.I., Traut, T.W. & Jones, M.E. (1981) in "Current Topics in Cellular Regulation - Biological Cycles" (Horecker, B. & Stadtman, E.R., eds.) Vol. 18, pp. 59-77, Academic Press, New York. Multienzymatic proteins in mammalian pyrimidine biosynthesis: Channeling of intermediates to avoid futile cycles.
89. Jones, M.E. & Christopherson, R.I. (1982) in "From Cyclotrons to Cytochromes: Essays in Molecular Biology and Chemistry" (Kaplan, N.O. & Robinson, A., eds.) pp. 611-672, Academic Press, New York. Some observations on the evolution of the regulation of the *de novo* pathway for UMP biosynthesis in procaryotes.
90. Christopherson, R.I. (1983) in "Methods in Enzymology - Enzyme Structure Part I" (Hirs, C.H.W. & Timasheff, S.N., eds.) Vol. 91, pp. 278-281, Academic Press, New York. Desalting protein solutions in a centrifuge column.
91. Christopherson, R.I. & Lyons, S.D. (1990) Medicinal Research Reviews 10, 505-548, John Wiley & Sons, New York. Potent inhibitors of *de novo* pyrimidine and purine biosynthesis as chemotherapeutic agents.
92. Christopherson, R.I. (1992) in "Biochemistry through Questions" (Kuchel, P.W. & Ralston, G.B., eds.), McGraw-Hill, Melbourne.
93. Christopherson, R.I. (1993) in "Biology" (Knox, R.B., Ladiges, P.Y. & Evans, B.K., eds.), McGraw-Hill, Melbourne. Information box in: DNA and chromosomes: their structure and replication.
94. Christopherson, R.I. (1995) in "Paths to Pyrimidines" an International Newsletter (Davidson, J.N., ed.), 3, 21-30, College of Medicine, University of Kentucky. The catalytic mechanism and potent inhibitors of dihydroorotase.
95. Christopherson, R.I., Williams, N.K., Schoettle, S.L., Szabados, E., Hambley, T.W. & Manthey, M.K. (1995) Biochemical S ciety Transactions, 23, 888-893. Inhibitors of dihydroorotase, amido phosphoribosyltransferase and IMP cyclohydrolase as potential drugs.
96. Christopherson, R.I. & Szabados, E. (1997) in "Channelling in Intermediary Metabolism" (Agius, L. & Sherratt, H.S.A., eds.), chapter 16, pp 315-335, Portland Press, London. Nucleotide biosynthesis in mammals.

97. Slaytor, M. & Christopherson, R.I. (1997) *in* Schaum's Outlines, Theory and Problems of Biochemistry, second edition, (Kuchel, P.W. & Ralston, G.B., eds.), Chapter 15, pp 419-457, McGraw-Hill, New York. Nitrogen metabolism.
98. Christopherson, R.I. (1998) in "Paths to Pyrimidines" an International Newsletter (Davidson, J.N., ed.), 6, 64-72, College of Medicine, University of Kentucky. Inhibitors of pyrimidine nucleotide biosynthesis as drugs.
99. Lal SP, Christopherson RI, dos Remedios CG (2002) Drug Discovery Today, 7 (18 Suppl): S143-9. Antibody arrays: an embryonic but rapidly growing technology.
100. Christopherson, R.I., Lyons, S.D. and Wilson, P.K. (2002) Acc. Chem. Res. 35, 961-971. Inhibitors of *de novo* nucleotide biosynthesis as drugs.
101. Christopherson, RI (2003) Encyclopedic Reference of Genomics and Proteomics in Molecular Medicine, Molecular Principles, Nucleotide Biosynthesis.

(v) Patents

98. Christopherson, R.I., Schmalzl, K.J. & Sharma, S.C. (1989) U.S.A. Patent Application No. 07/417,867. Production of 2-oxo-4-carboxy pyrimidines.
99. Christopherson, R.I., Schmalzl, K.J. & Sharma, S.C. (1987) Complete Patent Specification: Australia 77692/87, Japan 220095/87, U.S.A. 091,761, South Africa 87/6552, Europe 87307744.0. Enzyme Inhibitors.
100. Diefenbach, R.J., Szabados, E., Seymour, K.K. & Christopherson, R.I. (1996) Australian Provisional Patent Application P02795. Quantitative assay for antiphospholipid antibodies.
101. Christopherson, R.I. and dos Remedios, C.G. (2000) International Patent Application filed PCT/AU99/01156. ARIPO patent, Eurasian patent, European patent, OAPI patent, and 77 other national patents. An Assay.
102. Christopherson, RI, dos Remedios, CG, and Celermajer, DS (2002) PCT Int. Appl. 89 pp, CODEN: PIXXD2 WO 0223191. A1 20020321 CAN: 136: 229049, AN 2002: 220928. Immunological diagnostic device for systemic vasculature conditions.
103. Christopherson, R.I. and dos Remedios, C.G. (2002) United States Patent Application 20020019018, February 14. Assay to detect a binding partner.
104. Christopherson, R.I., Mackay, J.P., Matthews, J. (2002) Australian Provisional Patent filed 28/11/02. Therapeutic agents.

(vi) Recent Invited International Lectures

- *Immunophenotyping of leukaemias using a cluster of differentiation antibody microarray*, IBC meeting, Hamburg, September 2002.
- *Immunophenotyping of leukaemias using a cluster of differentiation antibody microarray*, IBC 13th International Conference on Antibody Engineering, San Diego, December 2002.
- *Consensus immunophenotypes for the common leukaemias using a CD antibody microarray*, IBC 4th Annual Protein Microarrays, San Diego, April 2003.
- *Cloning and expression of malarial pyrimidine enzymes*, Joint 11th International and 9th European Symposium on "Purines and Pyrimidines in Man", Egmond aan Zee, the Netherlands, June 2003.

(f) Teaching Innovations

- I was heavily involved in the development of the Graduate Medical Program (USydMP) about 5 years ago. I wrote many documents for this novel course based upon Problem Based Learning, and was the pre-clinical coordinator for the first case "Mr Sarich's Chest Pain", written with the Professor of Cardiology at Royal Prince Alfred Hospital, Prof. Phil Harris. The USydMP is web-based and students view details of the case of the week on computers in tutorial rooms. This first case was presented to the Australian Medical Council for accreditation of the course and is available to the public as "a sample week" of the course at

  http://www.gmp.usyd.edu.au/vguide/students/samplew/mscp_fset.html

- I have developed a new course "The Biochemistry of Cancer" for Biochemistry 3 students which covers current aspects of epidemiology, causes, molecular mechanisms and treatment. This course of 8 lectures has largely been developed from published work, some of the information is too recent to be found in text books.

- I have developed a Biochemistry 3 practical class experiment "Adenosine Deaminase Deficiency in Human Lymphocytes" which is run over 4 days. This experiment uses high pressure liquid chromatography (HPLC) with computerized data acquisition and processing. The emphasis is on using sophisticated equipment and software to link basic biochemical properties of cells with a clinical disorder.

(g) Administration, Service to the Profession and Community

- Foundation Head, School of Molecular and Microbial Biosciences University of Sydney (1998-03)
- Chair, Faculty Promotion Committee to Lecturer and Senior Lecturer, Faculty of Medicine (2000-02)
- National Committee for Biochemistry of the Australian Academy of Science (1991-97)
- Referee panel for the National Health & Medical Research Council
- Grants Evaluation Panel of the Australian State Cancer Councils
- Convenor and organizer, National Heads of Schools (Biochemistry) meeting, University of Sydney, September 2003
- Panel of reviewers for *Biochemistry, Biochemical Pharmacology* and *International Journal of Biochemistry and Cell Biology*

(h) Referees

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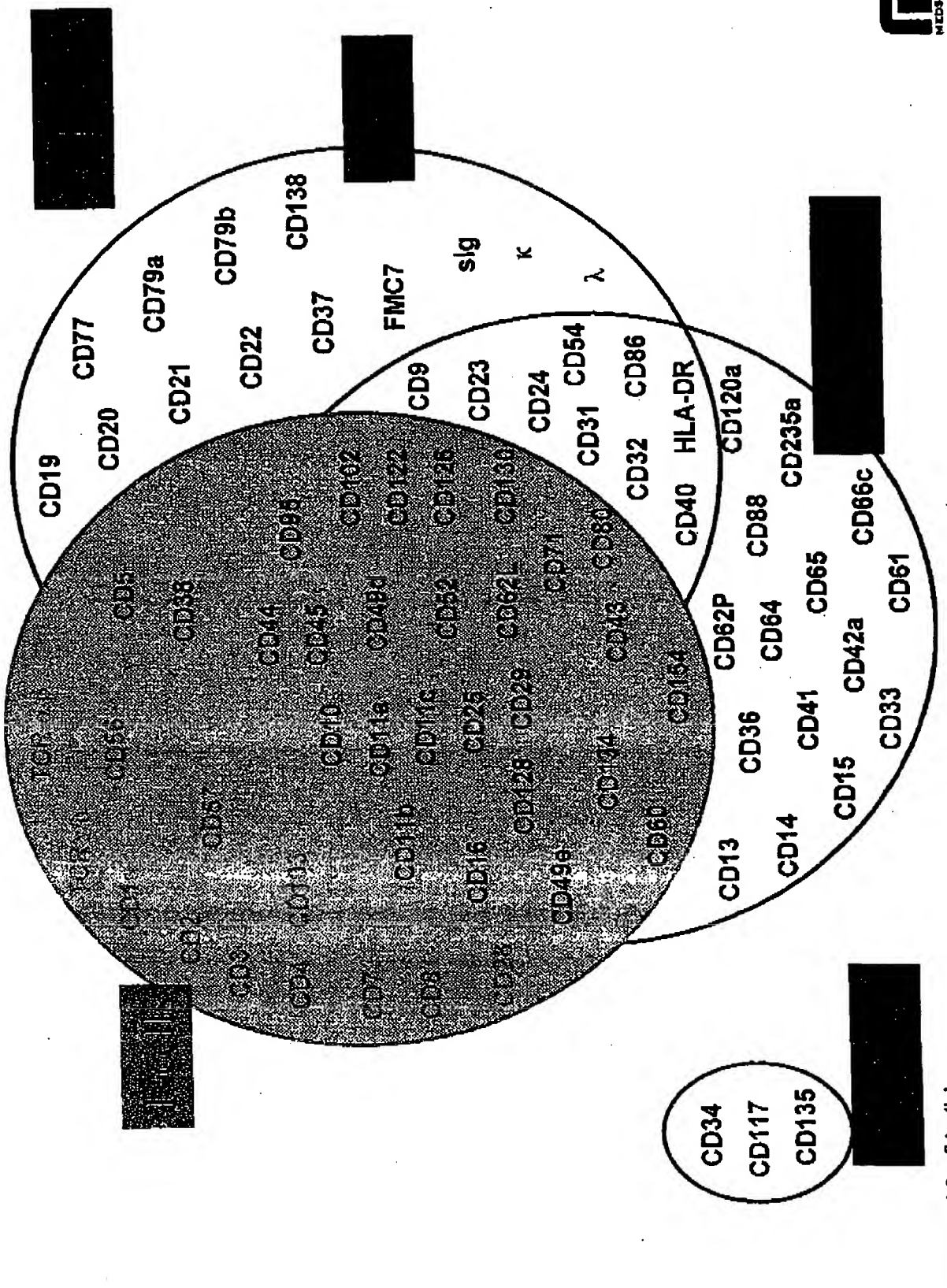
IN THE MATTER of United States
Patent Application No. 09/888,959
in the name of University of Sydney

This is **Exhibit RIC-2** referred to in the Statutory Declaration of
Professor Richard Ian Christopherson made on 10 February 2004 (date).

R. I. Christopherson


A T-cell Lineage Pattern
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MEDSAIC
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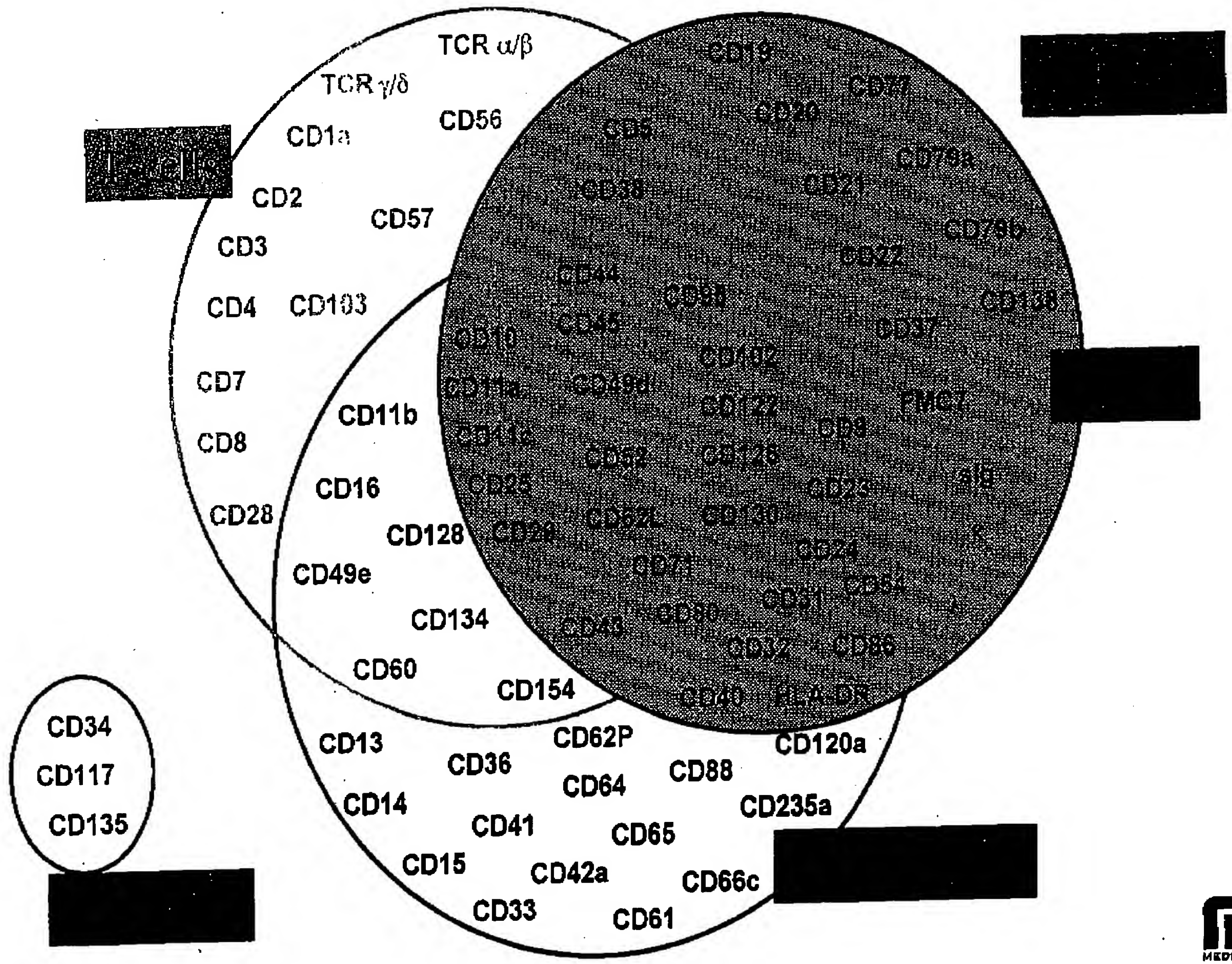
IN THE MATTER of United States
Patent Application No. 09/888,959
in the name of University of Sydney

This is **Exhibit RIC-3** referred to in the Statutory Declaration of
Professor Richard Ian Christopherson made on 10 February 2004 (date).

R. I. Christopherson

A B-cell Lineage Pattern



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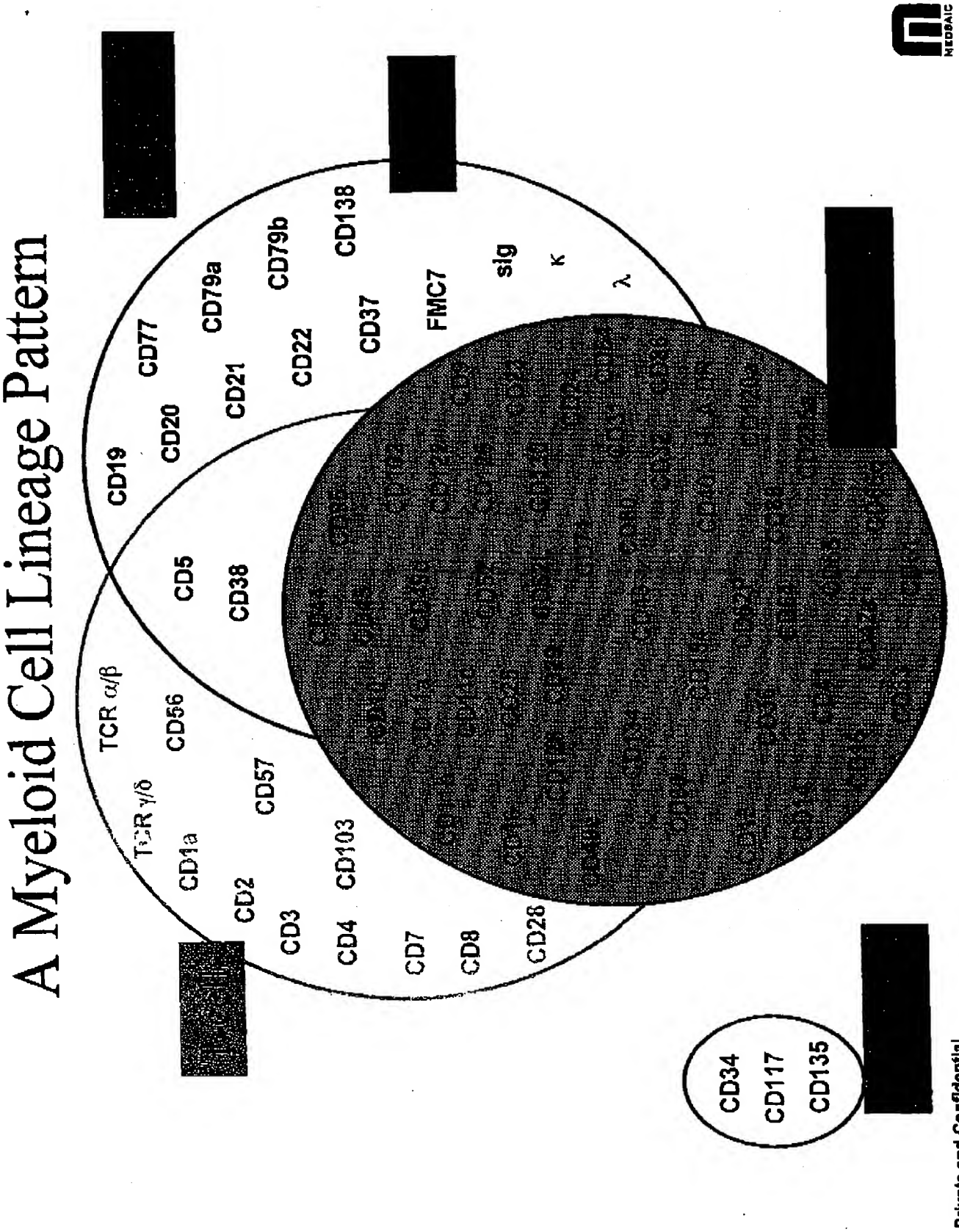
Patent Application No: 09/888,959
in the name of University of Sydney

This is **Exhibit RIC-4** referred to in the Statutory Declaration of
Professor Richard Ian Christopherson made on 10 February 2004 (date).

R. I. Christopherson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MEDAIC
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Macintosh HD:Documents:Dakara Folder:Attachments Folder:2422932 declaration.doc-10 February 2004

IN THE MATTER of United States
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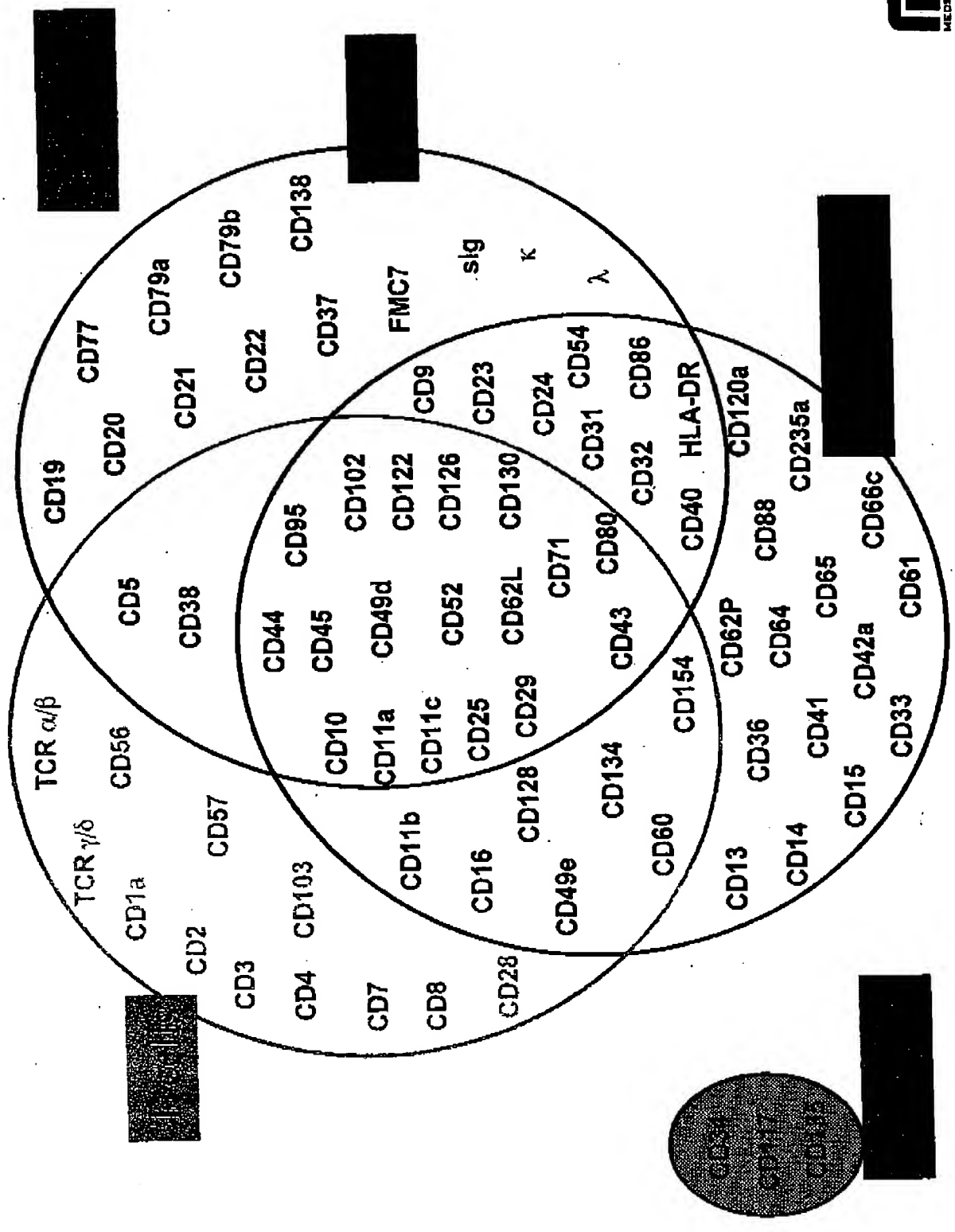
R. I. Christopherson



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